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Translation of "Kombinirovannoye vozdeystviye faktorov kosmicheskogo poleta na nekotoryye funktsii organizma"

Paper presented at the Second International Symposium on Basic Environmental Problems of Man in Space, Paris, 14-18 June, 1965

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON JUNE 1965

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EFFECTS OF THE COMBINED STRESSES OF SPACE FLIGHT ON CERTAIN BODY FUNCTIONS

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ABSTRACT

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The effect of space flight factors, acceleration, vibration, ionizing radiations, and the complex action of dynamic and radiation factors on some functions and oxidation metabolism of the central nervous system are considered. The combined effect of these factors on cell division in hematopoietic tissues, as well as the effect of acceleration on cerebral blood flow are studied.

The variety and complexity of the results of combined dynamic and radiation factors stem from numerous combined action mechanisms. The oxygen effect on the processes of cell division and on the reactions of the central nervous system cannot be ignored. Such factors as protective inhibition, parabiotic phenomena, origin of dominant foci, play a significant part in the central nervous system reactions to combined action. Author

The conditions to which living organisms are exposed during space /1* flight are unusual because several factors operate on them simultaneously or consecutively--acceleration and vibration, then weightlessness, and, inevitably, irradiation to a greater or lesser degree. This set of factors elicits an integral reaction of the body which can be studied from a variety of indices. A simple consideration of this general reaction reveals something about the extent of involvement of a given factor in the origin of certain functional changes. But this is not enough for analysis of the physiological mechanisms of the phenomena. Study of the reactions to the combined effects of several factors under actual space flight conditions must be supplemented by experimental simulation of the factors, singly and in combination, in laboratory.

Our earlier investigations showed, in line with other published data, that complex and sometimes unexpected reactions arise when different factors

*Numbers given in the margin indicate the pagination in the original foreign text.

are combined. In general the results of two different factors (whether acting simultaneously or consecutively) still cannot be predicted on the basis of the reaction elicited by each factor used by itself. For this reason we /2 thought it worthwhile to compare the effects of the individual factors and bombinations thereof applied at different times and with different intensities. In simulating these actions in the laboratory, we evaluated the reactions from a variety of functional indices.

Some of the matters examined in this report represent the joint efforts of a team of investigators, e.g., impairment of the hemodynamics of the central nervous system (related purely to altered gravitational conditions). Others, such as functions of the central nervous system, vestibular apparatus, oxidation processes, and cell division in hematopoietic organs are considered from the standpoint of the effects of both individual factors (acceleration, vibration, and irradiation) and various combinations thereof.

1. Effect of Dynamic Factors on Cerebral Hemodynamics and Central Nervous System Function

Under altered gravitational conditions significant impairment of general and, even more important, central hemodynamics is possible. There is a tendency to attribute some of the specific symptoms that arise after exposure to positive acceleration to changes in circulation. This applies, in particular, to impairment of vision and loss of consciousness. The filling of cerebral /3 vessels with blood was found to change significantly following a change in acceleration of as little as a fraction of 1 g (1, 2). On the other hand, to judge by oxygen saturation of venous blood, the cerebral blood flow remains constant during positive acceleration of about 4-5 g for 10 sec approx. (3). However, the investigations involved highly trained subjects. Despite the prevailing view, the few direct investigations on intracranial blood flow during acceleration indicate that cerebral hemodynamics is more resistant to positive accelerations than one might expect [4, 5, 6].

The mechanisms of stabilization of the cerebral blood flow have been linked to the balance of venous flow and shifts of fluid [7, 8]. Moskalenko, Benua, and Graunov [9] examined the matter from the theoretical standpoint. As the authors note, the curve showing filling of the cerebral vessels with blood is similar to that for a hydromechanical model only in the lower vertebrates. The physiological component can be clearly distinguished in analogous reactions in the higher animals and man, but the curve showing changes in blood filling differs significantly from the exponential.

The limit of compensation capabilities in cardiovascular reactions to acceleration can be clearly determined if visual disturbances are used as a criterion of brain blood supply deterioration. According to the literature, this symptom invariably appears when certain values of /4
acceleration and exposure are achieved [6], as if this phenomenon were determined by the interaction of purely mechanical factors.

Nevertheless, the state of cerebral hemodynamics is ultimately determined by the neuroreflex mechanisms. Futile attempts to demonstrate that there is a direct regulatory influence on the central vessels gave rise to the notion that the cerebral blood vessels constitute a self-regulating system affected by metabolic conditions [10, 11]. Some recent findings suggest that extracerebral reflex mechanisms influence the cerebral blood vessels [12]. If the resistance of the cerebral blood vessels to acceleration could be increased by training, it would be difficult to conceive of this process occurring without the participation of the central reflex mechanisms.

In our experiments on a centrifuge we subjected rabbits to positive longitudinal accelerations, about 5 g in the head region and about 10 g in the pelvic region. The cerebral blood flow was recorded in large vessels on the brain surface and in the anterior longitudinal sinus by means of a temperature-sensitive element. The animals received several 3-second exposures in succession at 30-minute intervals 5-12 times a day for a few days. The initial effects in all the animals were a brief, slight decrease in the blood flow, followed by a sharp decrease toward the end of the exposure.

Integral values of the cerebral blood flow were recorded with a different time constant, i.e., 12, 20, and 60 seconds. Fig. 1 shows the integral values of the blood flow for the 60 seconds during which a 30-second exposure took place. It is evident that there was no change in the blood flow on the first day of the experiment during the first centrifugation. Then the deviations with the + sign appeared, and by the end of the day with the same exposure there was a marked decrease in the blood flow. The blood flow decreased on the second day during the first exposure and it continued to decrease during subsequent exposures on the same day. After a 24-hour interruption, i.e., on the third day of the experiment, the reaction to the first exposure was positive; it became negative only during the later exposures. On the fourth day (with no interruption) the effect was much weaker and stabilization set in.

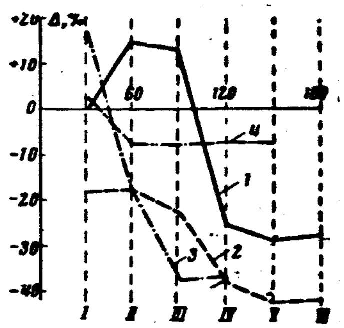

Fig. 1. Deviation of integral minute values of the cerebral blood flow from the mean level at rest. The data pertain to the rotation period in several successive actions for 4 experimental days (1, 2, 3, 4 - rotation days).

Abscissa - time in minutes

Roman numerals - ordinal numbers of the exposures during a single day

In Fig. 2, where abnormalities in the blood flow at the time of rotation are shown, the blood flow is integrated for 6-12 sec intervals. This diagram clearly shows the effects of cumulation and subsequent stabilization. The reaction intensified up to the 4th exposure, but weakened at the 5th. Then in order to "disrupt" the process of stabilization, the interval between exposures was shortened to 5 minutes. The reaction intensified and again stabilized at the 8th or 9th exposure. The reaction intensified again only after a lengthening of the exposure, when the reaction was once more subjected to the law of cumulation.

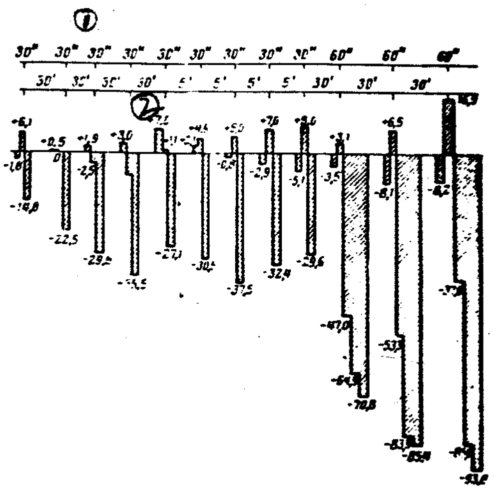

Fig. 2. Deviation in blood flow level from the mean level at rest in % at the moment of exposure with several successive loads during a single experimental day.

1 - Duration of rotation
2 - Interval

The complete pattern of the changes in cerebral venous flow in response to acceleration is shown in Fig. 3. It is evident that following a deep drop in blood flow toward the end of the exposure, a biphasic reaction set in after the centrifuge was halted. Thus, there was a difference in cerebral blood flow reaction to the same factor in the same object. The existence of mechanisms of physiological compensation responsible for this difference cannot be doubted. There also aeems to be a distinct relationship between the kind and level of reaction and the number and sequence of preceding actions. The central neuroreflex mechanisms on which the "readiness" of the entire cardiovascular system to withstand abrupt changes in circulation ultimately depends probably take part in these processes. Consequently, prolonged weightlessness may be an extremely adverse factor in that it reduces the adaptability of the cardiovascular system to changes in gravitational conditions. 16

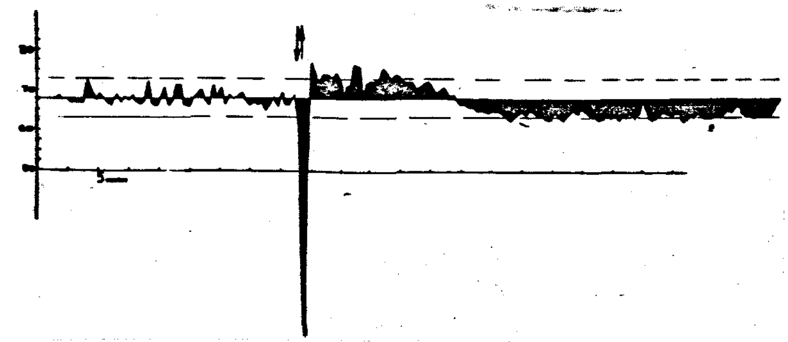

Fig. 3. Blood flow at the time of centrifugation; the area of deviations from the mean level at rest is darkened.

Besides acceleration, vibration plays a major role during the active part of the trajectory. We compared the effects of vibration, acceleration, and space flight on background bioelectric activity of the skeletal muscles and function of the otoliths. We performed experiments on guinea pigs, using as indices of vestibular function the electromyographic reaction of the extensors in the hind leg to adequate stimulation of the organ of equilibrium. Graduated rocking of the animal around the longitudinal axis of the body on a special apparatus for 10 sec (frequency 0.6 cps, angle of inclination 25°) was used as the stimulus.

The electromyograms were integrated and recorded in relative 17
units from the readings of an automatic meter simultaneously with the tracing on film. The animals were subjected to radial accelerations of 8 g in a back-chest direction created by rotation on a centrifuge for 15 minutes. There were 2 rotation periods 24 hours apart.
The electric activity of the skeletal muscles in a state of relative rest increased sharply (Fig. 4). However, the effect was brief, for on the next day, after the second centrifugation, myoelectric activity

decreased and from the 6th day on was virtually indistinguishable from the control.

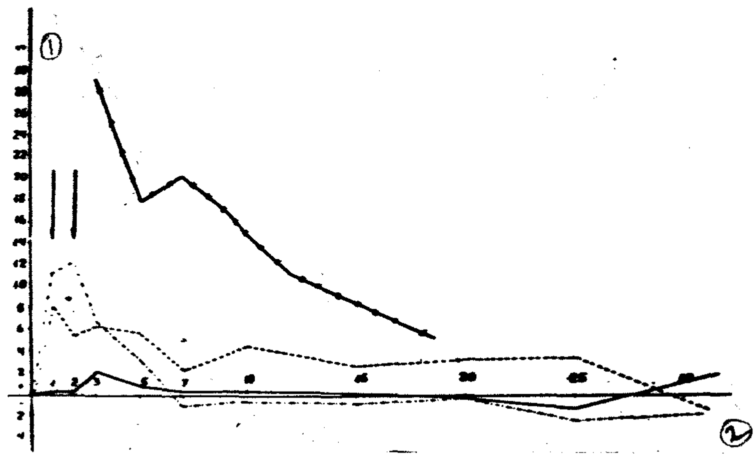

Fig. 4. Changes in integral background electric activity of muscles in the hind leg of guinea pigs after centrifugation and vibration and after flight on the Vostok.

Abscissa - time after exposure in days; ordinate - change in parameter under study in relative units; solid thin line - control animals; solid thick line with crosses - animals on board the spacecraft; dash line - animals exposed to vibration; dash-dot line - animals exposed to acceleration. The arrows designate the days when vibration or acceleration was applied.

1 - Electric activity in relative units; 2 - Days

After vibration at a frequency of 70 cps, amplitude of 0.4 mm, and duration of 15 min applied, as in the case of centrifugation, in 2 periods 24 hours apart, there were less distinct but more persistent changes. Normalization did not set in until at least 25 days after the initial exposure (Fig. 4).

The changes in background myoelectric activity of the guinea pig carried on Vostok 4 combined features of both factors and greatly exceeded them in effect (Fig. 4).

The latent period of the reaction of the skeletal muscles to adequate stimulation of the vestibular apparatus after centrifugation shortened during the first few days after exposure, but lengthened beginning the 10th day without showing any tendency to return to normal as long as 30 days after exposure (Fig. 5). The shortening of the latent period of this reaction after vibration was less abrupt but significant, and it /8
remained short for 25 days.

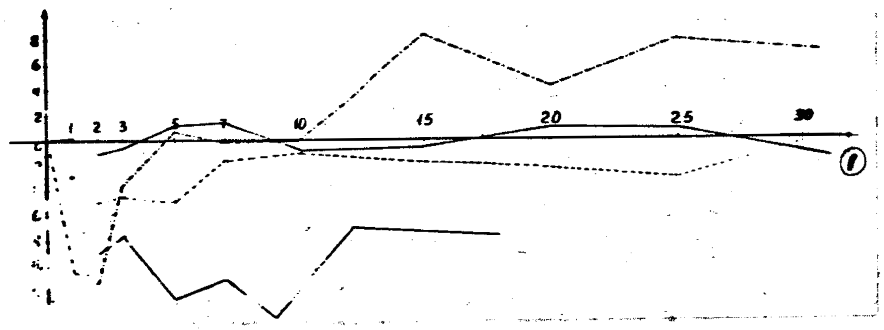

Fig. 5. Change in duration of the latent period of the reaction to adequate stimulation of the otoliths of the vestibular apparatus in guinea pigs after exposure to centrifugation and vibration and after flight on Vostok 4. Symbols the same as in Fig. 4.

1 - Days

In the guinea pig carried on the spacecraft, the latent period of the reaction decreased sharply for 16 days (Fig. 5). The opportunities for comparing the results of laboratory experiments with the data recorded in the animal on board the spacecraft are limited by the fact that the results of the laboratory experiments shown in the graphs were obtained from statistical material and averaged for the groups of animals, whereas there was just one guinea pig on board the spacecraft. However, the differences between the results of the experiments on this animal and on the groups of animals exposed to vibration and acceleration go far beyond the limits of individual and group spread. The results of this experiment convinced us that vibration may be an important element in the effect of space flight factors on several functions of the central nervous system.

Up to now the effect of vibration on the central nervous system has been studied mainly by industrial hygienists. The many works on the subject are summed up in monographs and evaluated in reviews of the literature [13, 14, 15, and others]. Many authors found that vibration causes inhibition in various divisions of the central nervous system with marked parabiotic phenomena.

We investigated the effects of vibration with the above-mentioned parameters on oxidation processes in brain tissue, motor defense reflexes, vestibulotonic reflexes, and conditioned activity. The state of the oxidation processes was judged from the partial pressure of oxygen (pO_2) and from the results of the so-called "oxygen sample". pO_2 was determined in a chronic experiment by the "oxygen cathode" method, which is based 19
on the principle of polarographic analysis [16]. Due to the electrochemical and mathematical validation of the method [17], it can be effectively used in experiments on animals. Experiments were performed in special gas chambers with a normal oxygen content (21%). The chambers were periodically ventilated with air containing a strictly measured amount of oxygen ("oxygen sample"). This took 10 sec.
We showed elsewhere that the increase in critical current due to change in oxygen concentration at the cathode as a result of this procedure is more or less proportional to the tissue consumption of oxygen at the electrode.

Unconditioned defense reflexes were investigated by Godin's and Gorshkov's method [18]. Three intensities of pain were used: (1) weak physiologically constant stimulation always equal to three times the threshold value; (2)physiologically constant stimulation of moderate intensity normally equal to the threshold value multiplied by 6; (3) physically constant stimulation of great force normally equal approximately to the threshold value multiplied by 10.

Conditioned reflexes were investigated by Kotlyarevskiy's motor-food method. /10

To exclude the influence of the noise that accompanied vibration, all the control animals were placed near the enclosed vibration stand during vibration of the experimental animals.

Changes in unconditioned defense and vestibulotonic reflexes produced by vibration were observed more than 12 days after a double exposure, and with respect to intensity of reaction, the effects were equal to those of whole-body gamma irradiation with lethal doses. The oxidation processes in brain tissue under the influence of vibration underwent phase changes. These experiments will be described in detail below.

Although the noise that accompanied the operation of the vibration stand had an initially inhibitory effect on conditioned activity in most of the animals, the difference between the experimental and control groups was quite distinct (Fig. 6) and statistically significant ($P < 0.01$). The decrease in conditioned reflexes resulted in numerous disturbances of the correct intensity relations. Some of the animals exhibited in rare instances a complete ultraparadoxical phase when there were no reactions to positive stimuli, whereas they reacted with a distinct food reflex to a non-reinforced stimulus.

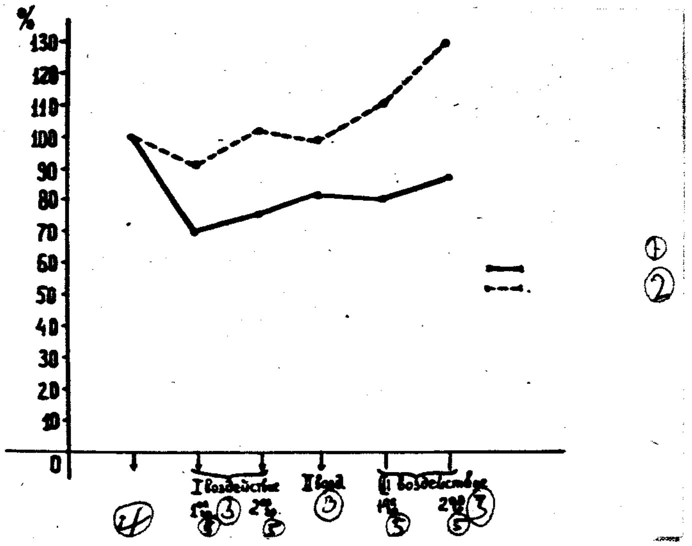

Fig. 6. Change in mean intensity of the conditioned reflex after exposure to vibration and noise on a vibration stand (simulated vibration).

Abscissa - group of experiments: background, Mean group value from the results of 20 experiments performed before exposure.

1st and 3rd exposures and 1st and 2nd groups. Mean group data from 6 experiments (1st and 2nd weeks after exposure). Interval between the 1st and 2nd exposures - 2 weeks; interval between the 2nd and 3rd exposures - 1 week.

Ordinate - intensity of the conditioned reflex expressed in % of the original level taken as 100%.

1 - Vibration
2 - Absolute vibration
3 - Background
4 - exposure
5 - group

2. Combined Effect of Vibration and Ionizing Radiation on Metabolism and Functions of the Central Nervous System

It was to be expected that vibration, which has such a marked influence on the functioning of the central nervous system, would also affect the latter's reaction to ionizing radiation. We investigated the combined effect of vibration and radiation on the oxidation processes in /11 brain tissues and on unconditioned defense and vestibulotonic reflexes. Experiments were performed on guinea pigs and white rats of the Wistar strain.

The animals were irradiated after general vertical vibration with the aforementioned parameters. The rats received 600 r of X-rays (whole body) 10-15 minutes after vibration (voltage 180 kV, skin focus distance 45 cm, filters Cu 0.5 mm + Al 0.75 mm, dose rate 22-43 r/min). The guinea pigs received 500 r 30-50 min after vibration (Co^{60} at a rate of 260 r/min).

The animals were divided into the following groups: (1) exposed to vibration, then to irradiation at the times mentioned above, and to vibration again 24 hours later; (2) exposed to vibration twice with a 24-hour interval between exposures; (3) irradiated in the indicated doses; (4) control. A total of 40 guinea pigs and 25 rats were the experimental animals and they were distributed almost equally between the various groups. The results were processed by the methods of nonparametric statistics (criteria χ-square and medians).

Irradiation altered the threshold of excitability of the flexor defense reflex. The changes were not statistically significant, but they had a definite tendency (Fig. 7 c) and did not correlate with the changes in value of the latent period of the response to physically constant stimuli. /12

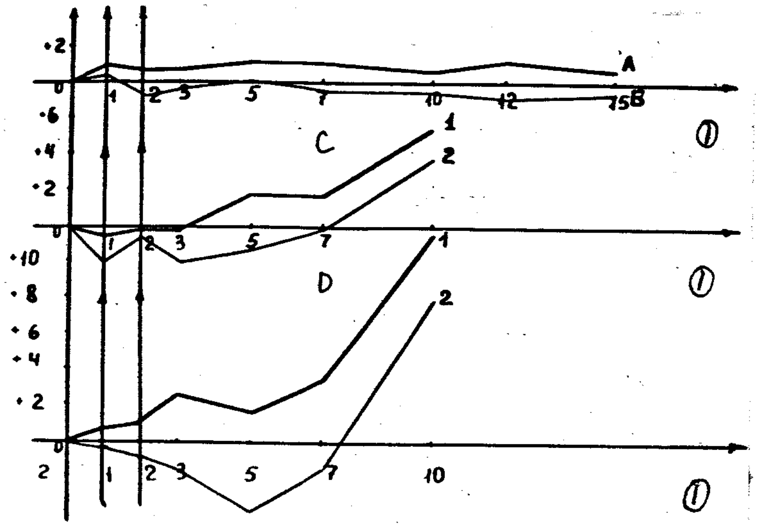

Fig. 7. Change in mean value of the threshold stimulus.

A - in animals exposed to vibration twice
B - in the control animals
C - in the irradiated animals
D - in the animals exposed to both irradiation and vibration

1 - group of animals exhibiting elevation of threshold of excitation
2 - group of animals exhibiting lowering of threshold of excitation

Abscissa - time in days
Ordinate - change in intensity of threshold stimulus in relative units
The arrows designate the days of exposure to the agents

1 - Days;

Under the influence of irradiation the latent period of the reflexes to the 3 types of stimulation lengthened considerably. The increase was statistically significant as compared with both the original background and the control animals. The greatest increase was shown by the latent period of the reflex to the weak stimulus; the smallest, to the strong stimulus. The reaction to the stimulus of moderate intensity occupied an intermediate position (Fig. 8). As a result, the number of experiments with postirradiation impairment of intensity relations not only did not increase, it decreased markedly, as in the control group.

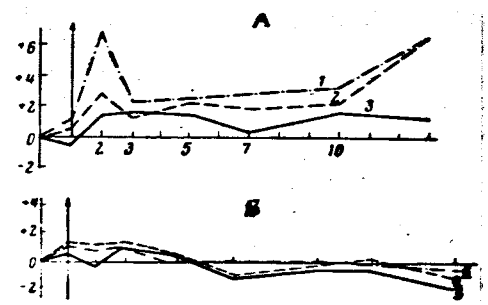

Fig. 8. Change in value of the latent period of the flexor reflex in A - irradiated animals; B - control. 1 - to the weak physiologically constant stimulus; 2 - to the moderate; 3 - to the strong physically constant stimulus.

Abscissa - time in days; ordinate - latent period in relative units

The arrows designate the days of irradiation

In the animals exposed twice to vibration, there was a slight but statistically significant elevation of the threshold of excitability (Fig. 7a).

The changes in threshold of excitability likewise did not correlate with the changes in latent period. The latter were quite sharp. The most typical change in the latent period due to vibration was impairment of the correct intensity relations.

Regarding the reactions to the weak stimulus, there was a tendency for the latent period to contract, whereas in the reactions to the moderate and strong stimuli, it tended to lengthen, especially in the case of the latter. Thus, there was impairment of intensity relations of the balancing phase type (Fig. 9).

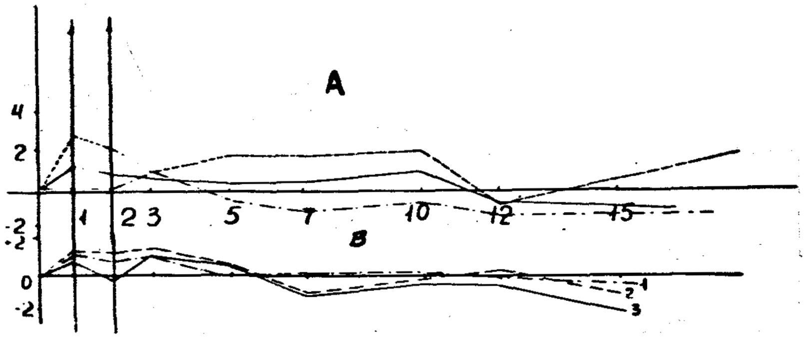

Fig. 9. Change in mean value of the latent period of the flexor reflex after two exposures to vibration.

A - mean value of the latent period in the experimental animals; B - in the control animals in the reactions to: 1 - weak physiologically constant stimulus; 2 - moderate; 3 - strong physically constant stimulus

Abscissa - time in days; ordinate - latent period in relative units

The arrows designate the days of vibration

The combined effect of vibration and irradiation produced a distinct but statistically insignificant change in threshold of excitability, which was similar to that observed in the irradiated animals. Under the influence of both irradiation alone (Fig. 7 c) and combined agents (Fig. 7 d) the changes in threshold of excitability proceeded in two directions. It rose in some of the animals while it fell in others. /13

The changes in latent period in the animals exposed to the combined agents included features of the reactions to vibration and to irradiation. In some of the animals exposed to the two agents, the effect of irradiation was predominant. The changes in latent period of the reactions to the weak stimulus were more pronounced than those of the reactions to the strong stimulus, while these of the reactions to the moderate stimulus occupied an intermediate position. As a result, the correct intensity relations between the reactions to the stimuli of different intensity were preserved (Fig. 10 a).

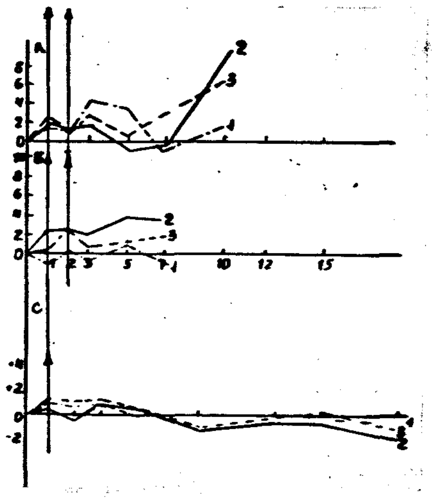

Fig. 10. Change in value of the latent period of the flexor reflex in the animals exposed to both vibration and irradiation.

A and B - mean value of the latent period from the groups of experimental animals in the reactions to:
1 - the weak physiologically constant stimulus;
2 - the moderate; 3 - the strong physically constant stimulus
C - similarly for the control group

Abscissa - time in days; ordinate - investigated parameter in relative units

The arrows designate the days of exposure: left - combined exposure to gamma radiation and vibration; right - only exposure to vibration

The changes in latent period in the group of animals exposed to the two agents were similar to those caused by vibration, although irradiation left its imprint on them. The value of the latent period of the reactions to the strong stimulus increased sharply from the very first day of exposure and it remained fairly high throughout the investigation (Fig. 10 b). The combined exposure here had about the same effect as vibration. The reactions of this group of animals to the weak stimulus were characterized, as it were, by an algebraic summation of the effects of irradiation and vibration. As we saw above, the effects of vibration and irradiation were diametrically opposite /14 (after vibration there was a tendency for the latent period to contract; after irradiation, to lengthen). In this group of animals the value of the latent period of the reflex to the weak stimulus remained unchanged. Thus, the lowering of excitability of the investigated reflex arc in this group of animals, as in those subjected to vibration, occurred at a low level and was of the balancing phase type. The only difference was that this tendency was somewhat more pronounced in the case of the combined exposure.

The effect of vibration and irradiation on excitability of the vestibulotonic reflex was diametrically opposite. Vibration increased it, as shown by contraction of the latent period of the reaction (Fig. 11) and prolongation of the aftereffect (Fig. 12). In the irradiated animals, the latent period of the reaction lengthened (Fig. 11) while the duration of the aftereffect shortened (Fig. 12). The vibration effect predominated in the animals exposed to the two agents for the first 5-6 days, but thereafter, as radiation sickness set in, the irradiation effect became dominant. It is interesting to note that between the 5th and 9th days (Fig. 12) the duration of the aftereffect in the irradiated animals scarcely differed from that in the control, where this index likewise decreased. However, in the animals exposed to the two agents, the effect of vibration was completely overcome at the aforementioned times.

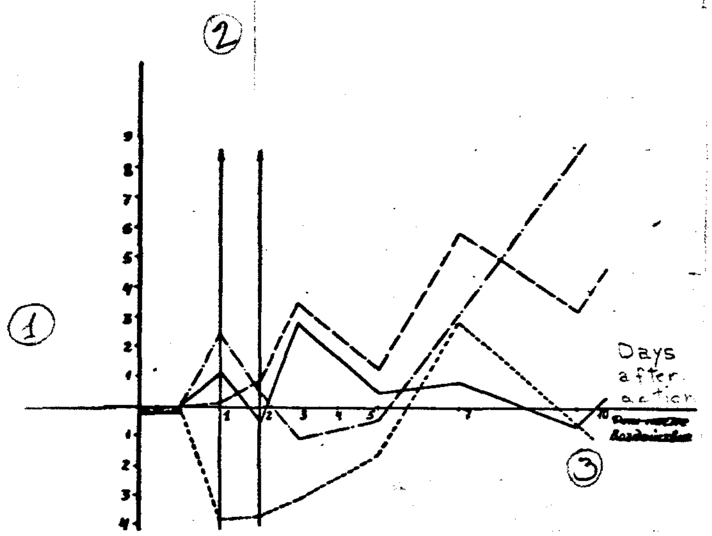

Fig. 11. Mean changes in duration of the latent period of the vestibulotonic reflex to test stimulation in guinea pigs after vibration, irradiation, and both combined.

Ordinate - value of the parameter under study, expressed in units of deviation from the mean norm prior to exposure and ratios to the mean group deviation prior to exposure

Abscissa - time from the start of exposure in days

I - arrow of vibration + irradiation
II - arrow of irradiation

Dash-dot line - group exposed to the combined action
Dash line - irradiated animals
Broken line - vibrated animals
Solid line - control group

1 - Value of the latent period in relative units
2 - Change in duration of the latent period of the reaction to test stimulation after exposure
3 - Days after exposure

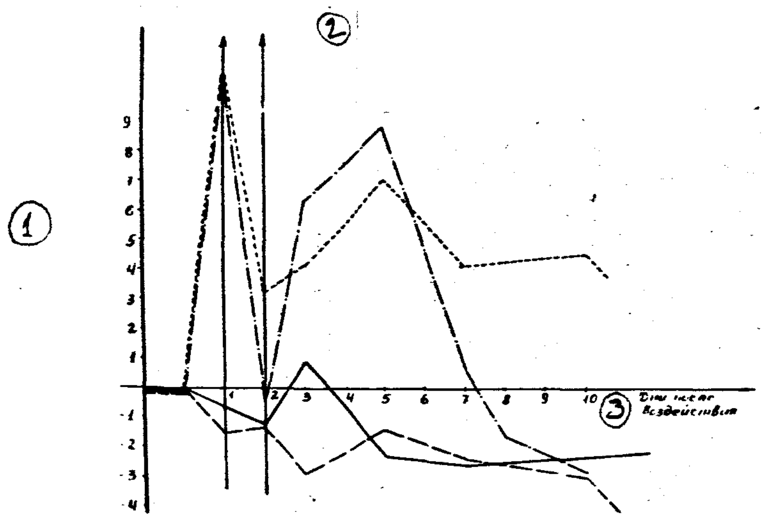

Fig. 12. Change in duration of the aftereffect of the vestibulotonic reaction of guinea pigs to test stimulation after vibration, irradiation, and both combined.

Symbols the same as in Fig. 11

1 - Duration of the aftereffect in relative units
2 - Change in duration of the aftereffect of the reaction to test stimulation after exposure
3 - Days after exposure

The combined effect of these factors on bioelectric activity /15 of muscles at relative rest was different. It is evident from Fig. 13 that irradiation caused a prolonged decrease in background myoelectric activity, whereas vibration caused a brief but very sharp increase. As a result of the combined action, the background myoelectric activity increased as it did after vibration, but the pattern of the changes resembled those in the irradiated animals. Therefore, the curve showing the changes in this parameter was almost a mirror reflection of the corresponding curve in the irradiated animals.

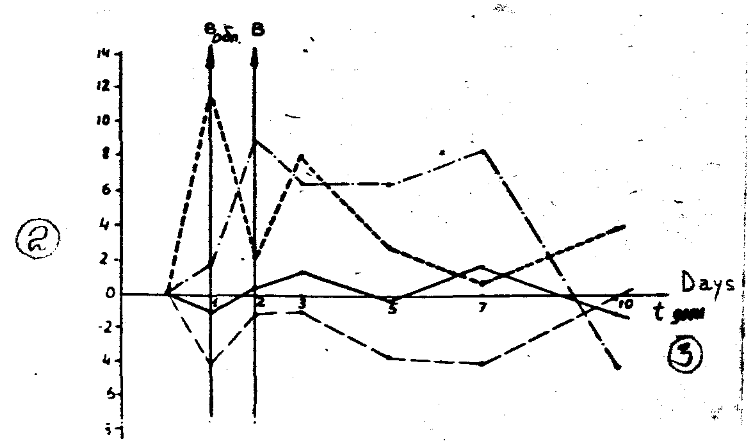

Fig. 13. Mean changes in background electric activity of the extensor muscles in the hind leg of guinea pigs after vibration, irradiation, and both combined.

Symbols the same as in Fig. 11

1 - Change in background myoelectric activity
2 - Electric activity in relative units
3 - Days

Fig. 13 shows that irradiation reduced the effect of vibration on the days when it was strong and intensified it when it was weak. The background myoelectric activity was maximal on the days of the initial examination after vibration, but it was much lower following the combined exposure. On the 7th day after vibration, myoelectric activity rose slightly, but after the combined exposure it was near the maximum. The intensity of the additional agent likewise seems to be significant for the resulting effect, This accounts for the mirror resemblance between the pattern of changes in these indices after the combined exposure and that observed in the animals exposed to only one of the factors.

Similar phenomena were noted when studying the effects of combined action of the factors on myoelectric activity during stimulation of the vestibular apparatus (Fig. 14). The relations here were the reverse. Vibration reduced myoelectric activity, while irradiation increased it. During the first two days the vibration effect predominated and after the combined exposure the index under investigation changed in the same direction as after vibration alone. On the 3rd and 5th days after exposure myoelectric activity changed in the same direction as in the irradiated animals, but here too the weak changes elicited by irradiation were intensified by vibration (Fig. 14, 3rd day) while the strong changes were weakened (Fig. 14, 5th day). These relations resemble the phenomena of dominant and parabiosis. /16

The phenomena of the dominant are also recalled by experiments described in the literature which showed that the typical radiation reactions are intensified when irradiation is combined with factors having a directly opposite effect. For example, an agent that causes leukocytosis may when combined with irradiation intensify leukopenia [19, 20, 21, 22, and others]. The effects of irradiation combined with burns on arterial pressure, excitability of the depressor and pressor reactions, etc. are very similar to parabiotic phenomena [21]. It is still unclear whether we are dealing here solely with an external chance resemblance between the described phenomena and the principles of parabiosis and dominant or whether these mechanisms play a major role in the combined radiation lesions. The matter requires experimental study

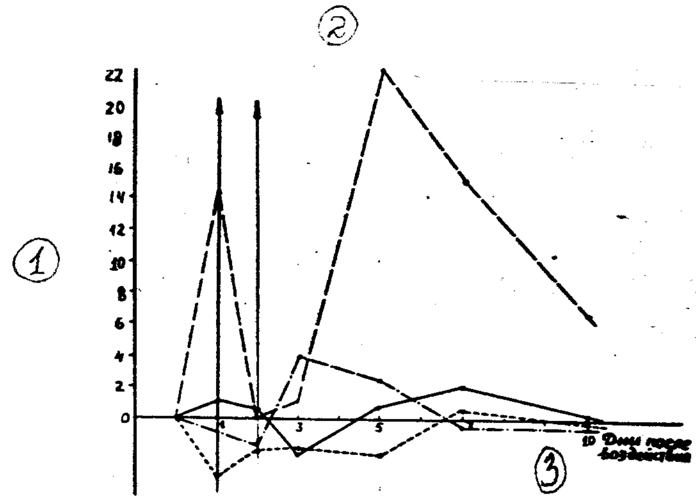

Fig. 14. Mean changes in electric activity of the extensor muscles in the hind leg of guinea pigs in response to adequate stimulation of the vestibular apparatus after vibration, irradiation, and combined exposure.

Symbols the same as in Fig. 11

Vibration followed by irradiation has a peculiar effect on the oxidation processes in different parts of the brain. An investigation of changes in oxygen tension and rate of consumption in brain tissues resulted in the indentification of three successive phases: (1) decrease in pO_2 and increase in oxygen consumption; (2) increase in pO_2 and decrease in oxygen consumption; (3) restoration period during which oxygen consumption by the tissues returns to normal. The first phase lasts 3-5 minutes. Toward the end of vibration or immediately afterward comes the second phase, which lasts 15-30 minutes and then gives way to the third phase, which sometimes lasts several hours. /17

Oxygen tension increased and rate of oxygen consumption occurred both after vibration and after irradiation. The process was much more pronounced after irradiation. Thus, vibration and irradiation depressed the oxidation processes in brain tissues. However, a combination of the two agents did not result in the summation of the same kind of effects.

In the animals subjected to irradiation after vibration, the changes in oxygen tension and rate of oxygen consumption were similar to those noted after vibration alone (Figs. 15, 16).

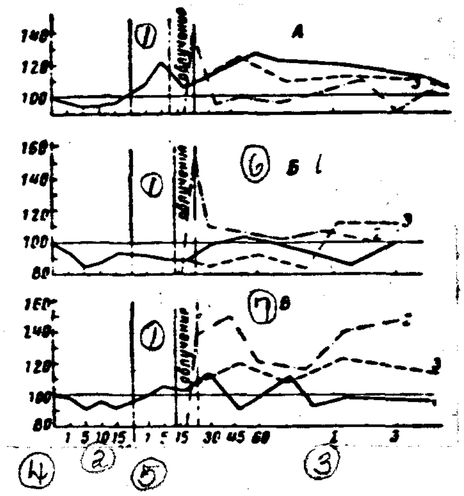

Fig. 15. Change in mean values I pr during vibration followed by irradiation.

A - auditory cortex
B - sensorimotor cortex
C - striopallidal formations

1 - animals subjected to vibration alone
2 - animals subjected to irradiation alone
3 - animals subjected to vibration and then irradiation

Abscissa - time in minutes and hours; ordinate - value of in % of the original backgrouhd

1 - Irradiation
2 - Minutes
3 - Hours
4 - Vibration
5 - After vibration
6 - B
7 - C

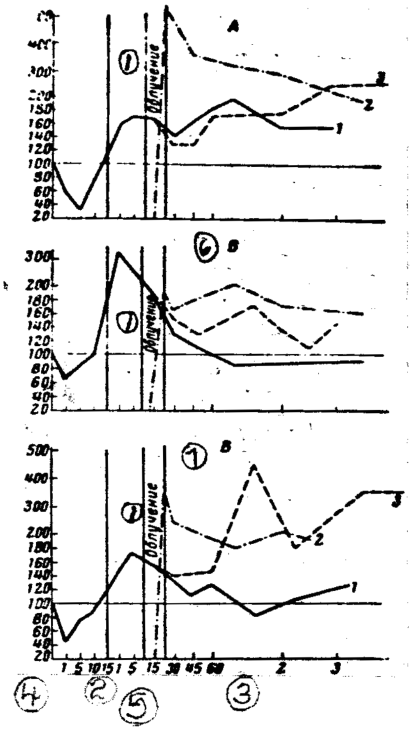

Fig. 16. Change in mean values ΔI_{pr} during and after the first vibration followed by irradiation.

1 - animals subjected to vibration alone
2 - animals subjected to irradiation alone
3 - animals subjected to vibration and then irradiation

Ordinate - value ΔI in% of the original background

Other symbols the same as in Fig. 15

1 - Irradiation
2 - Minutes
3 - Hours
4 - Vibration
5 - After vibration
6 - B
7 - C

The early changes arising from the effects of the second exposure to vibration on the day after irradiation likewise differed little from those observed in the animals subjected to vibration alone. But on the following days the pattern of changes in oxygen tension and /18 consumption in the animals exposed to both vibration and irradiation displayed some unusual features. There was a gradual decrease in oxygen tension in the brain of all the experimental animals after irradiation. In the animals exposed to the two agents, the changes in oxygen consumption were biphasic. During the first 48-96 hours after irradiation, the level of oxygen consumption changed in the same direction as in the animals subjected to vibration, but the amplitude was smaller. Thereafter, however, the changes were similar to those observed in the irradiated animals, coinciding in phases but of greater amplitude. It was only on the 12th day that there was a reaction opposite to that in the irradiated animals, i.e., a sharp decrease in the rate of oxygen consumption by brain tissues (Fig. 17). Thus, here too, as in the investigation of the effects of these factors on the duration of the latent period and aftereffect of the vestibulotonic reflex, the vibration effect was predominant in the first phase, the irradiation effect in the second.

An examination of Figs.15-17 fails to reveal a relationship between the changes in oxidation processes after combined exposure and the value of the effect of each of these factors applied separately. In this respect the reactions of oxidation metabolism in brain tissues differ significantly from the myoelectric reactions to these factors. Therefore, the explanation of the effects of the combined /19 exposure that we suggested above is not applicable to the changes in the oxidation processes, where it seems that the oxygen effect and the functional state of the central nervous system at the time of irradiation play a decisive role. The rats were irradiated 10-15 minutes after exposure to vibration. They were irradiated in the phase of marked depression of the oxidation processes. As already mentioned, our investigations of the unconditioned defense and conditioned food reflexes implied the development of inhibition in the central nervous system. It is quite likely that protective inhibition in the higher divisions of the brain along with the oxygen effect may play an important part in the absence of summation of the effects of vibration and irradiation on the oxidation processes.

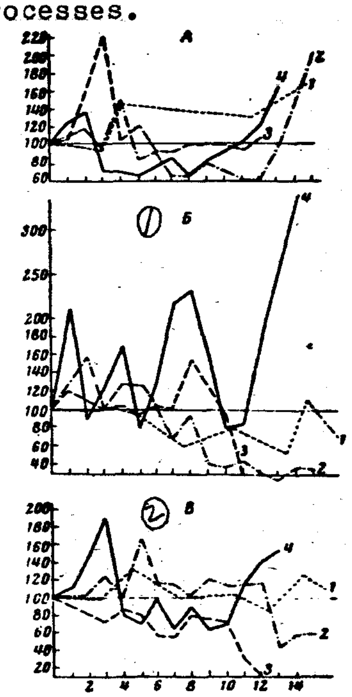

Fig. 17. Pattern of changes in mean values I_{pr} on different days in different groups of animals.

1 - control animals
2 - animals subjected to vibration alone
3 - animals subjected to irradiation alone
4 - animals subjected to vibration and then irradiation
Abscissa - time in days; ordinate - values in % of the original background. Other symbols the same as in Fig. 15

1 - B
2 - C

Numerous published reports show that the effects of combined ionization radiation and other factors are complex and varied. Many authors demonstrated that a combination of irradiation and mechanical, thermal, or other traumas results in mutual aggravation of lesions [19, 23, 24, 25, 26, and many others]. On the other hand, there have been cases in which a combination of irradiation and even very severe traumas not only did not result in summation of the effects, but at times mitigated the injury [27, 28, 29, 30]. Complex and varied effects have also been described in studies on the combined effects of irradiation and non-radiation factors on individual reactions.

When irradiation is combined with various kinds of traumas that cause leukocytosis, leukopenia is less marked than in the animals subjected to irradiation alone [31, 32, and others]. However, as noted above, /20
there have been cases in which additional agents that induce leukocytosis intensified leukopenia.

Although the protective effect of hypoxia is well known, certain factors that intensify the oxidation processes, e.g., moderate muscular activity during irradiation, before or after it, have a significant protective effect [33, 34, and others].

A survey of the extensive literature on combined radiation lesions was beyond the scope of this report. We merely cited some facts to show that the complexity and variety of the effects of vibration and irradiation that we observed are the rule rather than the exception when irradiation is combined with non-radiation factors. We ascribe this to the complexity and variety of the mechanisms involved in combined radiation actions.

This last matter has been inadequately studied, despite the extensive phenomenological material available in the world literature. I. R. Petrov [35] rightly states that activation of the protective and compensatory mechanisms plays a major role in the effects of combined exposure. These effects are also influenced by change in the humoral background of the organism and by summation of the effects on the central nervous system [26]. And some significance is attached to the stress reaction [36].

There are now concrete experimental data which show quantitatively the part played by the following mechanisms that may also be /21
significant in the phenomena that we observed:

(1) Oxygen effect (the literature on this subject is widely known so we can dispense with references);

(2) Change in functional state of the central nervous system [37, 38, 39, 40, and others];

(3) Change in functional activity of organs [41, and others];

(4) Change in mitosis in the tissues of various organs [42, and others];

(5) Change in reparative and compensatory processes [42, 35, and others];

(6) Effects of the interaction of irradiation and another factor on the course of individual reactions [43, and others].

The effects of the interaction of irradiation and other agents on the course of certain reactions -"algebraic summation" type up to complete elimination of the radiation reaction, observed following the action of irradiation and vibration on the latent period of the motor defense reaction in response to the weak stimulus - have also been noted when irradiation was combined with other factors. Specifically, similar facts were obtained in an investigation of red marrow following a combination of irradiation and bleeding [44, 45]. Despite the seeming simplicity of the phenomena, the underlying mechanism is still obscure.

It follows from the foregoing that vibration may significantly /22
alter both the metabolic and the functional reactions of the central nervous system to ionizing radiation.

3. Combined Effect of Dynamic Factors and Ionizing Radiation on Cell Division in Hematopoietic Organs

Study of the effect of space flight on the nuclei of mouse bone-marrow and splenic cells showed that space flight induces certain peculiar disturbances in the nuclei in the form of adhesion of chromosomes and slight increase in the frequency of aberrations. Ground experiments designed to determine the effect of vibration (35 and 70 cps for 60 minutes) on the hereditary structures of mouse bone-marrow and splenic cells revealed that vibration affects mitosis and produces irregularities comparable to those recorded after space flight. Centrifuge experiments on mice with accelerations ranging from 8 g for 5 and 15 minutes to 20 g for 5 minutes showed that this physical factor, like vibration, has a definite effect on the cell nuclei.

Analysis of the combined effect of acceleration, vibration, and X-irradiation showed that there is a relationship between the radiation effect and the actions to which the animals were exposed before or after irradiation. This investigation included a cytogenetic analysis of bone-marrow cells. A count was made of the number of normally dividing cells in the anaphase and telophase and of the number of

irregular mitotic figures - chromosome and chromatid bridges, bridges /23
with fragments, double and single fragments, and adhesion of chromosomes. Mitotic activity in the bone-marrow cells was evaluated from a count of at least 1000 cells in various stages of division and rest.

(a) Effect of acceleration. The effect of acceleration of 8 g for 5 and 15 minutes was described in an earlier study [46]. Mitotic activity in mouse bone-marrow cells remained within normal limits. A slight decrease occurred 4 hours after centrifugation for 5 and 15 minutes. The frequency of chromosomal aberrations after 1 and 4 hours was higher than in the control, chiefly with the 15 minute exposure. The greater frequency of injured cells is due to a higher rate of chromosome adhesions. The frequency of this impairment is directly proportional to the duration of the exposure.

This report presents the results of experiments on a centrifuge with acceleration of 20 g for 5 minutes. The experimental conditions were the same as in an earlier investigation [47]. Acceleration of 20 g seriously aggravated the condition of the mice at the end of the experiment. Some of the animals could not rise for 20 minutes or more. But their condition was satisfactory after a half-hour and they moved about in normal fashion.

Cytological analysis of the effects of acceleration of 8 g for 5 and 15 minutes and of acceleration of 20 g for 5 minutes showed /24
that the latter had a more depressant effect on mitosis in the experimental animals than it did in the controls. Regardless of the time the animals were sacrificed, the mitotic index was lower than the control, especially 4 hours after exposure (2.02 and 1.47 for the control and experimental animals, respectively).

The frequency of chromosomal aberrations with acceleration of 20 g, as in the experiment with acceleration of 8 g, was higher than the control due to an increase in the number of chromosome adhesions. The rate of chromosomal rearrangements in the experiment with acceleration of 20 g did not exceed than in the control. These changes in bone marrow persisted and they were higher than the control 2 days after exposure. Acceleration of 20 g also resulted in more numerous anaphases and telophases with large fragments. A similar phenomenon was noted in the earlier experiments with acceleration of 8 g.

Analysis of the results of exposure to different intensities of acceleration (8 g and 20 g) but for the same duration (5 min) showed an increase in the frequency of chromosome adhesions and aberrations with a lower mitotic index after exposure to 20 g. Exposures to 8 g for 15 minutes and to 20 g for 5 minutes had about the same effect, with the decrease in mitotic activity more pronounced after the 20 g exposure.

(b) Combined effect of acceleration and radiation. In this experiment mice were exposed to 100 r of X-rays at a rate of 11 r/min. /25
They were exposed to accelerations of 8 g for 15 minutes and of 20 g for 5 minutes 1 hour or 4 hours prior to irradiation. The animals were sacrificed 1 hour, 4 hours, and 48 hours after irradiation. The data obtained in these experiments were compared with the data obtained after X-irradiation with the same dose.

One hour after irradiation mitosis was low both after the combined action and after X-irradiation alone. Mitotic activity increased thereafter, but the process was much slower in all the experiments with the two factors, i.e., with centrifugation 1 and 4 hours before irradiation and with different rates of acceleration, it did not reach the level of mitotic activity in the control on the second day, unlike the experiment with irradiation alone.

A comparison of the results of the experiment with irradiation (100 r) alone with those of the experiment with acceleration of 8 g for 15 minutes followed by irradiation one hour later revealed a statistically significant number of nuclear irregularities 60 minutes after irradiation. Four hours after irradiation there was a significant decrease in both combined experiments 1 hour and 4 hours after centrifugation. Analysis showed that the decrease in number of nuclear /26 irregularities was due to a decrease in the frequency of true chromosomal aberrations - bridges and fragments. This was clearly evident 4 hours after the combined experiments ended. On the 2nd day the total number of nuclear irregularities both in the combined experiments and in the experiment with irradiation alone approached that in the control.

In the experiment with acceleration of 20 g for 5 minutes followed by irradiation with 100 r 1 hour and 4 hours later, there was a sharper decrease in mitotic activity initially (1 hour and 4 hours) than in the experiment with acceleration of 8 g followed by irradiation. When the animals were first sacrificed (1 hour), the number of chromosome adhesions in the combined experiments with irradiation after 1 and 4 hours was higher than in the experiment with irradiation alone. The frequency of all the chromosomal aberrations was close to that observed when the 100 r dose was used. However, there was a marked decrease in the number of chromosome bridges and some increase in the rate of fragmentation as compared with the results of radiation alone. Subsequently (4 hours) the number of adhesions was somewhat higher in the combined experiment, but the frequency of chromosomal aberrations was significantly lower than after irradiation alone. This decrease persisted in the combined experiments whether irradiation was applied 1 hour or 4 hours after acceleration.

On the second day, the frequency of all the irregularities in all the experiments (combined and irradiation alone) approached that in the control. However, just as in the combined experiment with acceleration of 8 g, mitotic activity remained lower in the experiment with acceleration of 20 g followed by irradiation than in the control. A comparison of the results of accelerations with different intensities (8 g and 20 g) followed 1 hour and 4 hours later by irradiation showed that in the experiment with acceleration of 8 g and irradiation 1 hour later, the total number of irregularities observed during the first two days the animals were sacrificed was much higher than in the experiment with acceleration of 8 g and irradiation 1 hour later. When irradiation was applied 4 hours after acceleration, the decrease was the same regardless of the intensity used before irradiation. The result was the same with regard to frequency of chromosomal aberrations after exposures of different intensities, as is evident from Figs. 18 and 19. As for adhesion of chromosomes, this irregularity in the combined experiments with acceleration of both 8 g and 20 g prior to irradiation was more frequent than in the experiment with irradiation, provided that the latter followed 1 hour after centrifugation (Fig. 20). When irradiation was applied 4 hours after centrifugation of either 8 g or 20 g, the frequency of adhesions exceeded that in the control only in the animals sacrificed 1 hour later. /27

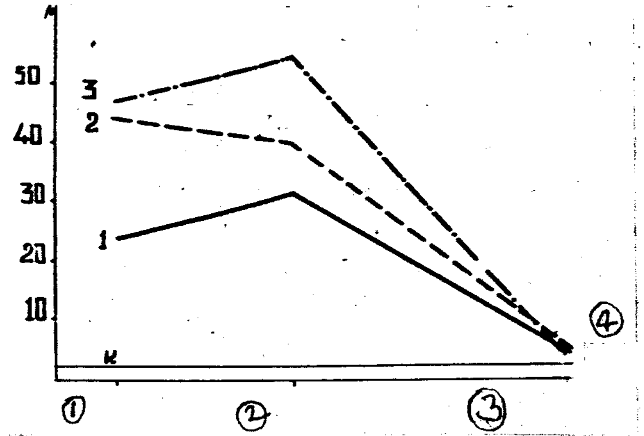

Fig. 18. Percentage of chromosomal aberrations in mouse bone-marrow cells after accelerations of 8 g and 20 g followed 1 hour later by X irradiation with 100 r

1 - centrifugation with acceleration of 8 g for 15 minutes and irradiation with 100 r
2 - centrifugation with acceleration of 20 g for 5 minutes and irradiation with 100 r
3 - X irradiation with 100 r

1 - 1 hour
2 - 4 hours
3 - 48 hours
4 - periods when animals were sacrificed

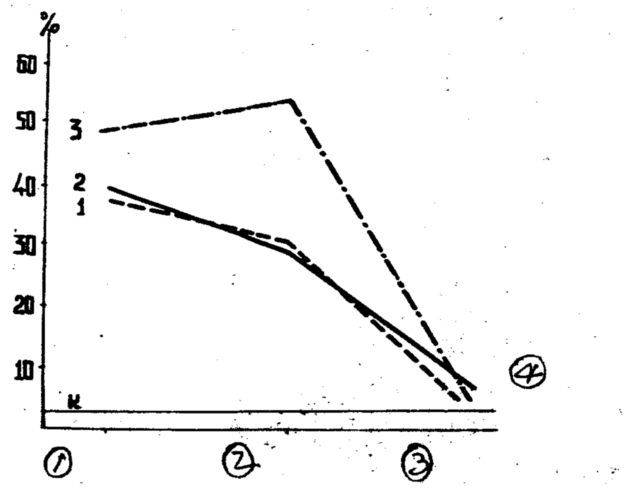

Fig. 19. Percentage of chromosomal aberrations in mouse bone-marrow cells after accelerations of 8 and 20 g followed 4 hours later by X irradiation with 100 r

1 - centrifugation with acceleration of 20 g for 5 minutes and irradiation with 100 r
2 - centrifugation with acceleration of 8 g for 15 minutes and irradiation with 100 r
3 - X irradiation with 100 r

1-4 - same as in Fig. 18

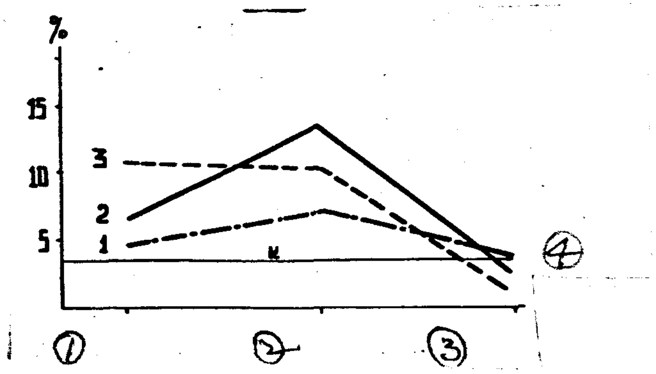

Fig. 20. Frequency of chromosome adhesions (%) in mouse bone-marrow cells after acceleration of 8 and 20 g followed 1 hour later by X irradiation with 100 r

1 - X irradiation with 100 r
2 - centrifugation with acceleration of 8 g for 15 minutes and irradiation with 100 r
3 - centrifugation with acceleration of 20 g for 5 minutes and irradiation with 100 r

(c) Combined effect of vibration, acceleration and 350 r of radiation. When investigating the combined effect of vibration or acceleration with irradiation, the question arose of how long the decrease in radiation effect lasts and whether it occurs with large doses of radiation (350 r). To determine the effect of the combined action at later periods and after using a large dose of radiation, we performed experiments involving the use of vibration and radiation, acceleration and radiation, and radiation followed by either vibration or acceleration. The control /28 was mice exposed to vibration, acceleration, or radiation alone.

Animals were vibrated under the following conditions: 700 cps with an amplitude of 0.005 mm for 60 minutes, resulting in an average acceleration of 10 g.

Other animals were subjected to acceleration of 10 g for 30 minutes on a centrifuge.

X-irradiation with 350 r at the rate of 11 r/minute was carried out

24 hours after vibration or centrifugation, or the animals were subjected to vibration or centrifugation 24 hours after irradiation. It was to be expected that such a large dose as 350 r would have a depressant effect soon after exposure, especially on such a sensitive organ as bone marrow. Obviously, deviations in the effect of radiation when combined with vibration or acceleration would most likely be manifested more distinctly some time after the end of the experiment. Hence, unlike the case in the earlier experiments, the animals were sacrificed 3, 7, 15, and 30 days after exposure.

The methods of cytogenetic analysis of injury to the nuclei of bone-marrow cells were the same as those used in the earlier investigations. A biological control was employed at the same time.

On the 3rd day there was no decrease in frequency of nuclear irregularities in the experiment with centrifugation or vibration before irradiation as compared with the effect of irradiation alone. The fre- /29
quency of true ahromosomal aberrations decreased slightly, mainly owing to a slower rate of fragmentation. For example, whereas in the experiment with irradiation alone (350 r) the percentage of fragments was 11.4, in the experiment with acceleration followed by 350 r of radiation the percentage of fragments was 5.3, and in the experiment with vibration followed by 350 r of radiation it was 7.1%. However, on the 7th day the total number of irregularities after the combined action was 50% below that found after exposure to irradiation (350 r) alone. The difference was significant. The results of this combined action, i.e., an actual decrease in radiation effect, are even more pronounced if the frequency of true chromosomal aberrations

is compared because the frequency of chromosome adhesions in both cases of combined action was higher than in the experiment with irradiation. In the experiment with irradiation the frequency of true aberrations was 18.12%; in the experiment with acceleration of 10 g before irradiation, 4.67%; in the experiment with vibration followed by irradiation, 5.50% (Fig. 21). On the 15th day the radiation effect actually decreased only in the experiment with preliminary vibration (700 cps) chiefly because of the decreased frequency of fragmentation and chromosome bridges. On the 30th day the results of the combined action and the action of irradiation alone were similar, but in all the experiments the number of nuclear disturbances was still much higher than the control. (It will be recalled that in the experiments with exposure to 100 r of radiation, as early as the 2nd day the frequency of disturbances was the same as in the control).

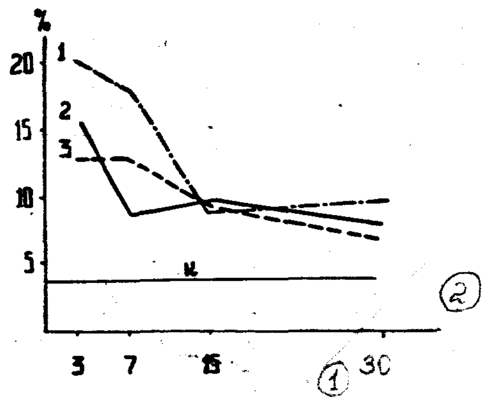

Fig. 21. Percentage of chromosomal aberrations in mouse bone-marrow cells after acceleration of 10 g or vibration at 700 cps followed by X irradiation with 350 r

1 - irradiation with 350 r
2 - vibration at 700 cps and irradiation with 350 r
3 - centrifugation with acceleration of 10 g and irradiation with 350 r

1 - 30 days
2 - periods when animals were sacrificed

This experiment confirmed our findings during earlier periods of sacrifice of animals on the decrease in radiation effect when exposure came 1 hour /30 or 4 hours after centrifugation or when the dose used was 100 r. In this experiment the decrease was noted on the 7th and 15th days.

In the second experiment of this series, the dynamic factors were applied 24 hours after irradiation with 350 r. There was higher mitotic activity than in the experiment with preliminary acceleration or vibration, especially during the first period the animals were sacrificed on the third day. There was also a decrease in the radiation effect judging by the frequency of chromosomal aberrations after the combined action as compared with the effect of radiation alone, but this decrease was insignificant on the 3rd day and significant on the 7th day. On the 15th and 30th days the effect was the same whether after irradiation alone or after a combination of factors, but in all cases it once again exceeded the frequency of nuclear irregularities in the control (Fig. 22).

The data on chromosomal aberrations in the bone-marrow cells of mice exposed to centrifugation or vibration are further evidence that these agents injure the nuclei by causing the chromosomes to adhere together and thus possibly help to form false bridges and fragments. Accelerations of 8 g and 20 g for the same length of time (5 minutes) reduced mitotic activity below that in the control, especially after acceleration of 20 g while increasing the frequency of chromosome adhesions and aberrations. The main difference between the effects of accelerations of 8 g and 20 g is that the latter reduced mitotic /31 activity more sharply.

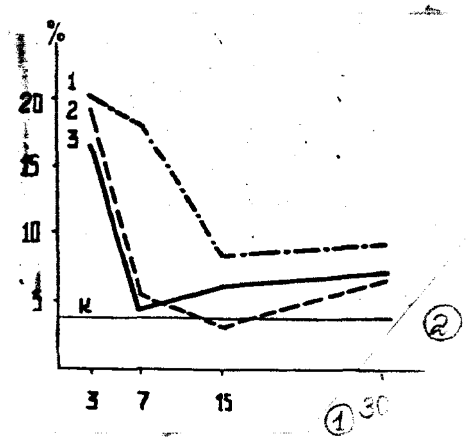

Fig. 22. Percentage of chromosomal aberrations in mouse bone-marrow cells after X irradiation with 350 r followed by acceleration of 10 g or vibration at 700 cps

1 - irradiation with 350 r
2 - irradiation with 350 r and centrifugation with acceleration of 10 g
3 - irradiation with 350 r and vibration at 700 cps

1 - 30 days
2 - periods when animals were sacrificed

The data on the combined action revealed a relationship between manifestation of the radiation effect and the agents to which the animals were subjected either before or after irradiation. The radiation effect was found to decrease more sharply in the experiments with preliminary centrifugation or vibration and less sharply in the experiments when these agents were applied after irradiation.

In all the experiments with the combined action, regardless of the radiation dose used, the radiation effect was reduced owing to the decrease in frequency of true chromosomal aberrations and above all fragments. However, the time when this peculiar effect appeared varied both with the time of the action prior to irradiation and with the intensity of the dynamic factors and radiation dose.

In the experiment with acceleration of 8 g for 15 minutes followed an hour later by irradiation with 100 r, the number of chromosomal aberrations decreased 50% within an hour. The same result was obtained in the experiment in which irradiation was applied 4 hours after centrifugation. Mitotic activity in the combined experiments remained below that in the experiment involving irradiation alone.

Acceleration of 20 g followed 24 hours later by irradiation with 100 r produced /32
an analogous effect on the number of chromosomal aberrations, particularly when there was a 4 hour interval between the two agents.

In the experiments with acceleration of 10 g or vibration at 700 cps followed by irradiation with 350 r, an actual decrease in the radiation effect judging by the frequency of chromosomal aberrations occurred only on the 7th and 15th days after irradiation.

In the case of combined actions, where irradiation is followed by a dynamic factor, the interval between the two as well as the radiation dose are highly significant. For example, in our experiment, the interval between irradiation with 350 r and acceleration of 10 g or vibration at 700 cps was 24 hours. A significant decrease in the radiation effect judging by the frequency of true chromosomal aberrations occurred on the 7th day, whereas in an experiment by Demin [48], in which vibration at 60 cps immediately followed irradiation with 100 r, it occurred after 5 hours and 2 days.

Radiation in doses of 100 r or so is known to depress and lengthen the cell cycle, while a dose of 200 r or more halts cell division temporarily. We showed that centrifugation and vibration, especially with acceleration of 20 g, influence mitosis in bone-marrow cells.

When two depressants are combined (e.g., radiation and dynamic factors), the cell cycle is extended even more and the time when the effect is manifested varies with the intensity of the factor and the radiation dose, either as soon as the experiment is finished or at varying intervals thereafter. However, in all cases there are definite effects, i.e., decrease in frequency of chromosomal aberrations due to the radiation dose and adhesion of chromosomas. It may be that the adhesion of chromosomes caused by dynamic factors partly helps to heal the breakages resulting ~~from~~ subsequent irradiation, thereby reducing the possibility of recombinations. On the other hand, when irradiation precedes the application of a factor, chromosome adhesion may prevent some aberrations from occurring or it may promote the healing of potential breakages arising from radiation. In either case this is suggested by the decrease in fragments and chromosome bridges in all the experiments. /33

The development of chromosome adhesion during the 2nd or 3rd day after centrifugation or vibration and the reduced effect of radiation after 7 days apparently mean that the presynthesis or synthesis stages of DNA are the phases of the cell cycle that are most sensitive to centrifugation or vibration. However, in analyzing the data one must bear in mind that such factors as acceleration and vibration impair the normal physiology of animals in different ways [49, 50]. Soviet and foreign investigators [51, 52, 53, 54, 55] have shown that acceleration impairs respiration and blood circulation in animals, resulting in reduced vital capacity, accelerated respiration rate, slowing of blood flow, and decrease in pulmonary ventilation. The oxygen supply of the tissues and organs is also impaired. It is possible that these changes /34 have some effect on the animals' bone-marrow oxygen supply, thereby reducing the radiation effect. However, disturbances in the cell need not arise only from changes in oxygen uptake especially since oxygen pressure in the intercellular substance of bone marrow is very low (11 mm Hg) as compared with that in subcutaneous tissue (55 mm Hg).

It must also be remembered that impairment of the oxygen supply may give rise to reflexes, specifically, to sharp stimulation of the sympathetic systems with the liberation of considerable amounts of epinephrine and norepinephrine. These two hormones are known to have pronounced protective action against radiation, although they strongly depress mitosis. The depressant effect persists until the prophase so that the cells do not start mitosis; they remain in the stage preparatory to mitosis.

If such physical factors as centrifugation or vibration are used, /35
especially with great intensities, the cell apparatus may be affected directly - displacement of chromosomes, their ejection from the spindle, and, finally, adhesion of chromosomes in different stages of the cell cycle.

Thus, normal division may change either under the influence of the organism itself due to hormonal and immunological action or artificially because of a variety of physical and chemical factors. This is evidently the result of depression of some process that prepares the cell for division and interferes with the function of the mitotic apparatus. The duration of the action of the factors or disruption of cell metabolism may also lead to prolongation of the cell cycle, suppression of DNA synthesis, and development of chromosomal aberrations.

The foregoing indicates that the different physiological changes induced by acceleration or vibration may impair cell division, which, in turn, may alter the effect of radiation.

Summary

1. This report examines the effect of acceleration, vibration, ionizing radiation, and the combined effect of dynamic and radiation factors on some functions and oxidation metabolism of the central nervous system and on cell division in hematopoietic tissues.

2. The hemodynamic factor plays a part in the reactions of the /36
central nervous system to acceleration. Acceleration causes marked changes in the cerebral blood flow resulting from the interaction of mechanical and physiological factors. Cumulation is a factor in these reactions. Training can increase the resistance of the cerebral blood flow.

3. Vibration (700 cps) induces changes in oxidation metabolism and functional state of the central nervous system. The oxidation processes intensify during exposure but undergo phasic changes in the aftereffect. Inhibition with parabiotic phenomena develops in various divisions of the nervous system under the influence of vibration.

4. Following the combined action of vibration and acute whole-body irradiation with lethal doses, the effect of vibration on the vestibulo-tonic reflexes and oxidation processes in brain tissues is generally predominant soon after exposure while the effect of irradiation is predominant at later periods. Changes in the latent period of the defense flexor reflex are characterized by predominance of the

effect of vibration or radiation in different groups of animals.

5. In cases where the effects of irradiation and vibration were in opposite directions, there was considerable variety. There were instances in which the result of the combined action was in between the effects of each of the factors separately (the latent period of the defense reaction to the weak stimulus). Sometimes the direction of the reaction to the combined factors reflected the vibration effect /37 while the dynamics of the reactions duplicated the pattern of the reactions to irradiation (change in background bioelectric activity of the muscles).

6. The changes in oxidation processes in brain tissues under the influence of vibration and irradiation were in the same direction. But there was no summation of the effects when both factors were combined.

7. Accelerations of 8, 10, and 20 g or vibration at 700 cps cause irregularities in mouse bone-marrow cell division in the form of chromosome adhesions and slight increase in frequency of aberrations. The dynamic space flight factors reduce mitotic activity in bone-marrow cells compared with that in the control, and the effect may persist for 30 days. The dynamic factors and irradiation influence bone-marrow cell division in the same way. However, when two factors are combined, the radiation effect decreases.

8. The combined action of accelerations of 8 or 20 g followed by irradiation with 100 r results in a marked crease in the radiation effect judging by the frequency of chromosomal aberrations when analyzed 1 hour and 4 hours later. There is a definite relationship between the manifestation of this decrease in effect, time of action prior to irradiation

(1 hour or 4 hours), and intensity of the dynamic factor).

9. The combined effect of acceleration of 10 g or vibration at 700 cps before irradiation with a dose of 350 r reduces the radiation effect judging by the number of chromosomal aberrations) 7 and 17 days /38 after irradiation.

10. If acceleration of 10 g or vibration at 700 cps follows irradiation with 350 r, a less pronounced decrease in the radiation effect occurs only on the 7th day after the experiment is over.

11. Cytological analysis made after 1 month in experiments with combined action revealed an actual increase in the frequency of nuclear irregularities as compared with the control, an indication of the persistence of radiation inhibition.

12. A combination of dynamic factors and irradiation produces complex and varied effects. These cannot be predicted from a knowledge of the effect of each of these factors when applied separately. When a dynamic factor and irradiation have unidirectional effects, there may be an absence of summation of the effect or even a significant weakening or distortion of the radiation reactions. When the effects are multidirectional, weakening or intensification of the effects, predominance of the dynamic or radiation factor, complex combination of effects, etc. are possible.

13. The variety and complexity of the results of combining dynamic factors and irradiation stem from the numerous mechanisms of combined action. The oxygen effect plays an important part in the combined action of the factors in question on the processes of cell division and on the reactions of the central nervous system. In addition,

the direct action of the dynamic factors on the chromosomes and the /39 indirect influence of changes in some physiological functions have an important bearing on the changes in cell division. The reaction of the central nervous system to a combined action is greatly influenced by protective inhibition, origin of dominant foci, parabiotic phenomena, and some other factors.

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